REMARKS

Claims 1-5, 7-9, 12, 13, 15, 18, 20 and 22 are pending in the application. By this amendment, claim 5 has been canceled, claims 1, 3, 4, 7, and 18 have been amended and new claims 30 and 31 have been added.

By this Amendment, Applicants amend claims 1, 3, 4, 7, and 18. These amendments are formal in nature and fully supported by the Specification as originally filed. Specific support can be found at page 13, paragraph 40, page 14, paragraphs 44-45, page 15, paragraph 52, page 21, paragraph 83 and page 24, paragraphs 94-95. New claim 30 is supported at page 24, paragraph 95, line 6. New claim 31 is supported at paragraph 207 (eukaryotic expression systems), and paragraphs 0093-0114 (heterologous antigens). No new matter has been added.

Reconsideration of the application is respectfully requested in view of the above amendments to the claims and the following remarks. For the Examiner's convenience and reference, Applicants' remarks are presented in the order in which the corresponding issues were raised in the Office Action.

Objections to the Specification

The specification was objected to as including some unclear symbols. In addition to those pointed out by the Examiner applicants noted two other examples and the specification has been amended to correct these clerical errors.

Rejections Under 35 U.S.C. § 112

Claims 1, 3-5, 7, and 18 stand objected to under 35 U.S.C. § 112, second paragraph, as being indefinite.

Applicants appreciate the Examiner pointing out what could be considered to be informalities in the claims and have responded to such by amending the claims to place them in proper form under 35 U.S.C. §112, second paragraph. Applicants have noted the Examiner's position with respect to these objections and have made a diligent effort in order to address and

overcome each of the objections by specific claim amendments. Applicants respectfully request withdrawal of these grounds for rejection.

Should the Examiner find that minor informalities remain within the claims, as amended, or should the Examiner prefer alternate language, Applicants are willing to discuss with the Examiner any suggestions for further amendments which would place the application in condition for allowance.

Rejections Under 35 U.S.C. § 102(e)

Claims 1-5, 7-9, 12-13, 15, 18, 20 and 22 stand rejected under 35 U.S.C. § 102(e) as allegedly anticipated by Curtiss et al. (US Pat. No. 6,383,496; hereinafter "the Curtiss '496 patent").

Applicants respectfully traverse this ground for rejection as the cited reference (Curtiss) is not "prior" art for the following reasons:

The present application claims priority to U.S. Application Serial No. 09/241,951 ("'951 Application") filed February 2, 1999. The '951 Application supports the claimed invention.

US Pat. No. 6,383,496 to Curtiss issued from U.S. Application Serial No. 09/314,062 ("'062 Application") which was filed on May 18, 1999, AFTER the filing of the '951 Application.

Applicants further note that Curtiss (U.S. Application Serial No. 09/314,062) is a "continuation-in part" of earlier filed U.S. Application Serial No. 08/970,789 ("'789 Application," filed November 14, 1997, now issued as U.S. Patent No. 6,024,961). The Curtiss '789 Application has an earlier filing date than the present Application. However, the Curtiss '789 Application **does not include** any disclosure related to the Dam gene which the Examiner referenced from the Curtiss '496 patent. In fact, the Curtiss '789 Application does not include any mention of the Dam gene or teach or suggest an attenuated live bacteria with an altered Dam gene.

The Curtiss '496 patent cited by the Examiner was based on the Curtiss '062 Application which was filed on a date subsequent to the filing date of the present Application. The '062 Application is a C-I-P of a Curtiss '789 Application which does not disclose the Dam gene or its

attenuation. Accordingly, the disclosure of the Curtiss '496 patent does not constitute "prior" art under 35 U.S.C. §102(e).

For these reasons, Applicants respectfully request that this ground for rejection under 35 USC § 102 be withdrawn.

CONCLUSION

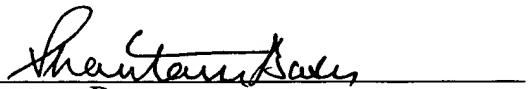
In light of the Amendments and the arguments set forth above, Applicants earnestly believe that they are entitled to a letters patent, and respectfully solicit the Examiner to expedite prosecution of this patent application to issuance. Should the Examiner have any questions, the Examiner is encouraged to telephone the undersigned.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned "**Version with markings to show changes made**".

With respect to all amendments and cancelled claims, Applicants have not dedicated or abandoned any unclaimed subject matter and moreover have not acquiesced to any rejections and/or objections made by the Patent Office. Applicants reserve the right to pursue prosecution of any presently excluded claim embodiments in future continuation and/or divisional application.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, Applicant petitions for any required relief including extensions of time and authorizes the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket no. 220002060724.

Respectfully submitted,

Dated: November 22, 2002 By: 

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Specification:

Please replace paragraph [0067] on page 17 with the following paragraph:

[0067] Figure 3 is a graphic representation illustrating that Dam regulates *in vivo* induced genes. [✋]β-galactosidase expression from *S. typhimurium ivi* fusions in Dam^+ and Dam^- strains grown in LB. The vertical axis shows [✋]β-galactosidase activities (μ-moles of o-nitrophenol (ONP) formed per minute per A_{600} unit per milliliter of cell suspension x 10^3).

Please replace paragraph [0068] on page 18 with the following paragraph:

[0068] Figure 4 is a graphic representation illustrating that Dam represses PhoP activated genes. [✋]β-galactosidase expression from *S. typhimurium ivi* fusions grown in minimal medium. The vertical axis shows [✋]β-galactosidase activities (μ-moles of o-nitrophenol (ONP) formed per minute per A_{600} unit per milliliter of cell suspension x 10^3). The *Dam* genotype is shown below the horizontal axis, and the *phoP* genotype is shown as black ($PhoP^+$) and gray ($PhoP^-$) boxes.

Please replace paragraph [00244] on pages 67-68 with the following paragraph:

[00244] All bacterial strains used in this study were derivatives of *S. typhimurium* 14028 (strain **1**). Mutant strains were isogenic to wild type and were obtained or constructed as described (*Dam102*::Mu*d*-Cm and *mutS121*::Tn*10* alleles are in LT2 (strain **7**), a highly attenuated (virtually non-pathogenic) strain as shown in Table 2, were obtained from Dr. John Roth (University of Utah) and Dr. Tom Cebula (The Food and Drug Administration), respectively; these alleles (and additional alleles below) were transduced into virulent strain, 14028, constructing strains **2** and **5**, respectively. *Dam[✋]Δ232* (strain **3**) was constructed using internal oligonucleotides that serve as PCR primers designed to construct an in-frame 300 bp deletion of defined *Dam* sequence. *dcm1*::Km was constructed according to (Julio, S. M., *et al.*, *Molec. Gen. Genet.*, **258**: 178-181 (1998)); the Km resistance determinant is associated with an internal deletion of >600 bp of *dcm* sequence. The *lrp31*::Km is a null insertion in the *lrp* gene

(strain **6**). The Dam overproducing strain (strain **4**) contains *E. coli Dam* on a recombinant plasmid (pTP166) in a wild-type background (Marinus, *et al.*, *Gene*, **28**:123-125 (1984).

Please replace TABLE 1 on page 70 with the following rewritten TABLE 1:

TABLE 1

Strain	Genotype	Oral LD_{50}	I.P. LD_{50}	Competitive Index (I.P.)
1	"wild type"	$>10^{+5}$	<10	---
2	*Dam102::Mud-Cm*	$>10^{+9}$	$>10^{+4}$	$<10^{-4}$
3	*Dam[]Δ232* (non-polar deletion)	$>10^{+9}$	$>10^{+4}$	$<10^{-4}$
4	wild type, (pTP166) (Dam overproducer)	10^{+8}	$>10^{+4}$	$<10^{-4}$
5	*mutS121::Tn10*	10^{+5}	ND	0.9
6	*lrp31::Km*	10^{+5}	ND	10.0
7	LT2	ND	$2 \times 10^{+4}$	ND

In the Claims:

1. (Amended) An immunogenic composition, comprising:

a pharmaceutically acceptable excipient; and

an attenuated form of live bacteria with a DNA adenine methylase (Dam) activity altered relative to the Dam activity of the wild-type, [activity of an] unaltered, pathogenic form of the live bacteria, with the alteration being in a manner which renders the live bacteria attenuated; and

a first heterologous nucleotide sequence operatively inserted in the live attenuated bacteria which first heterologous sequence expresses a heterologous antigen.

3. (Amended) The immunogenic composition of claim 1, further comprising:

a second heterologous nucleotide sequence wherein the Dam activity is altered by [a] the second heterologous nucleotide sequence.

4. (Amended) The immunogenic composition of claim [1] 3, wherein the first heterologous sequence is operatively inserted into a first [expression cassette] plasmid and further wherein the second heterologous sequence is operatively inserted into a second plasmid.

7. (Amended) The immunogenic composition of claim 1, wherein the live attenuated bacteria is altered relative to its wild-type form by a genetically engineered change in its DNA which change is a non-lethal, non-reverting mutation which renders the bacteria attenuated.

18. (Amended) The immunogenic composition of claim 1, wherein the heterologous antigen is an antigen of a microorganism which causes a [sexual] sexually transmitted disease.

Claim 5 is cancelled.

Claims 30 and 31 are added.